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Network Pharmacology in Different Disorders

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ABSTRACT: Network pharmacology is an emerging systems-based approach that explores how drugs and bioactive compounds interact with multiple molecular targets and biological pathways rather than focusing on a single target. It integrates pharmacology, bioinformatics, systems biology, and computational tools to understand the complex mechanisms underlying disease progression and therapeutic interventions. This study reviews the principles, methodologies, applications, advantages, and limitations of network pharmacology and highlights its role in the investigation of complex diseases. The approach combines target prediction, protein–protein interaction analysis, pathway enrichment, molecular docking, and experimental validation to identify key therapeutic targets and signaling pathways. Applications in breast cancer, osteosarcoma, chronic obstructive pulmonary disease (COPD), coronary heart disease (CHD), and polycystic ovarian syndrome (PCOS) demonstrate the ability of network pharmacology to reveal multi-target and multi-pathway mechanisms of natural compounds and herbal formulations. Studies involving Thymus vulgaris, Curcuma longa, hesperetin, Xuefu Zhuyu Capsule, and Sutaehwan show how bioactive compounds regulate pathways related to inflammation, apoptosis, oxidative stress, angiogenesis, metabolism, and hormonal balance. By providing a holistic understanding of drug actions and disease networks, network pharmacology supports drug discovery, drug repurposing, personalized medicine, and the scientific validation of traditional medicines. Overall, it represents a powerful framework for developing effective multi-target therapeutic strategies for complex chronic diseases.

III. INTRODUCTION:

Network pharmacology is an interdisciplinary approach to drug discovery and therapeutic research that studies how drugs interact with multiple targets within biological networks rather than focusing on a single target .The concept was formally introduced by Andrew L Hopkins in 2007. He described network pharmacology as a paradigm shift from reductionist pharmacology to a reductionalist pharmacology to a system based model for understanding drug actions.

Network of pharmacology is the new discipline has emerged which attempts to understand drug actions and interactions with multiple targets .it uses computational power to systematically catalogue the molecular interactions of a drug molecule in a living cell .Network of pharmacology appeared as an important tool in understanding the underlying complex relationships between botanical formula and the whole body . It also attempts to discover new drug leads and targets and to repurpose

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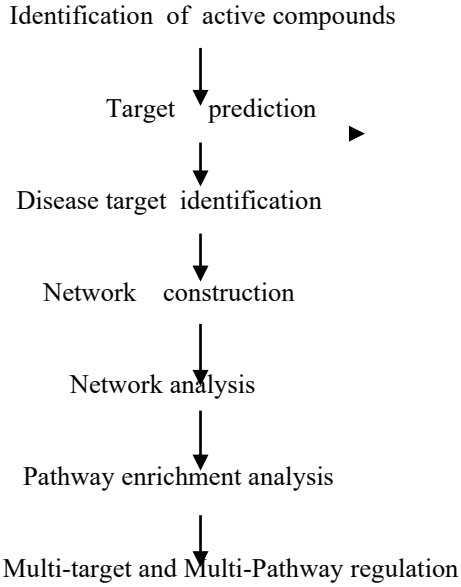
existing drug molecules for different therapeutic conditions by allowing an unbiased investigation of potential target spaces . Network pharmacology is based on the interaction of multiple disciplinary concepts including molecular biology ,biochemical biology and bioinformatics .Network pharmacology has gained more interest due to high success rate in clinical investigation ,less or affordable side effects ,enhanced drug efficacy ,regulation of the signaling pathway with multiple channels ,interaction of multiple genes and protein that could be easily be targeted causing the disease.In addition , network pharmacology also helps in finding the disease node which is an important disease node. It also increases the clinical candidate with potency and reduces the attrition rate in the disease network.

CONCEPT AND SIGNIFICANCE: The efforts of molecular biology and genomics research have provided large data which helped in gaining new insights into drug discovery processes. Hopkin, the father of Network pharmacology explained that a single drug can target multiple nodes in the disease network. Complex diseases such as cancer, diabetes, neuro degenerative disorders and cardiovascular diseases involve multiple genes, proteins and signaling pathways .It mainly studies how drugs interact with biological networks instead of isolated molecular targets .The core concept of network pharmacology is that diseases are not caused by the malfunction of a single gene but by perturbations in entire biological network. In this approach ,different types of network such as drug target networks .protein –protein interaction networks, gene regulatory networks and pathway networks are constructed and analysed using graph theory and computational tools. Important nodes often called hub genes or key targets are identified through topological analysis ,and pathway enrichment analysis is performed to understand the biological mechanisms involved.

The significance of network of pharmacology lies in its ability to improve drug discovery and therapeutic strategies. It plays a crucial role in studying complex diseases where multiple signaling pathways interact simultaneously .It supports polypharmacology meaning a single drug can modulate multiple target which is particularly important in cancer and chronic inflammatory diseases.

MECHANISM OF ACTION:



Methods In Network Pharmacology:

The drug target interaction: The identification of drug target interaction is considered as a key area of interest. The interaction of small molecules with different pharmaceutically important protein targets modulate its activity .The application of various biological assays for the high through put screening of large chemical databases enabled the identification of drugs with different targets . Chemical genomic research aimed to relate the chemical spaces with genomic spaces however ,the relationship of chemical and genomic is very limited. The experimental determination of compound protein interactions or potential drug –target interactions is time consuming and cost effective.

Prediction of drug –target interaction networks via chemical and genomic spaces: In 2008, Yamanishi proposed three computational methods for predicting drug–target interactions: the nearest profile, weighted profile, and bipartite graph learning methods, using chemical and genomic information from the Super Target and KEGG LIGAND

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databases. Among these, the bipartite graph learning method is the most effective because it can predict interactions for previously unseen drug compounds and target proteins without requiring three-dimensional protein structures. Unlike the nearest and weighted profile methods, which rely on structural or sequence similarity and may produce false positives, the bipartite graph approach is suitable for large-scale screening of drug candidates and target proteins.

Prediction of drug-target interaction networks through side effect similarity: Drug side effects often result from interactions with both primary and off-target proteins. While off-target interactions can cause harmful effects, they may also reveal new therapeutic uses, as seen with sildenafil, which was originally developed for angina but later used to treat erectile dysfunction. Researchers such as Monica Campillos demonstrated that drugs with similar side effects often share common protein targets, leading to the discovery of new drug–target interactions. Similarly, Feixiong Cheng developed the Meta ADEDB database to analyze adverse drug events and uncover novel pharmacological networks and potential therapeutic targets, highlighting the value of side-effect data in network pharmacology and drug repurposing.

Prediction of drug –target interaction networks by integrating the pharmacological space into chemical and genomic space: In 2010, Yamanishi proposed a novel computational method for predicting drug–target interactions by integrating chemical structure, pharmacological effects, genomic information, and drug–target network topology. The study demonstrated that drug–target interactions are more closely associated with pharmacological effect similarity than with chemical structure similarity. The method first infers pharmacological information from a compound's structure and then predicts drug–target interactions using pharmacological effect similarity within a bipartite graph framework. Its performance was validated across major protein classes, including GPCRs, ion channels, enzymes, and nuclear receptors. Unlike earlier approaches based on side-effect similarity, which are limited to marketed drugs, this method can predict pharmacological information and potential targets for both approved drugs and novel drug candidates.

Prediction of drug-target interaction via chemical protein interactome: Because many drug candidates fail during development, drug repurposing offers a cost-effective strategy by utilizing existing safety and pharmacokinetic data. Using chemical–protein interactome analysis, researchers identified genetic factors associated with adverse drug reactions and predicted drug–target interactions. Feixiong Cheng further developed target-based similarity inference, drug-based similarity inference, and network-based inference (NBI) methods, with NBI and its weighted variants showing improved accuracy in predicting new drug targets across major protein classes such as GPCRs, ion channels, enzymes, and nuclear receptors.

Prediction of drug- target interaction through a network-based random walk with restart on the heterogeneous network: The Network-based Random Walk with Restart on a Heterogeneous Network (NRWRH) predicts drug–target interactions by integrating drug–drug similarity, protein–protein similarity, and known drug–target interaction networks. Unlike traditional random walk methods, NRWRH operates on a heterogeneous network containing multiple biological data sources, enabling more effective prediction of novel drug targets. A key advantage of this approach is its ability to identify potential targets for drugs with no previously known targets by utilizing information from structurally similar drugs and their known interactions.

Prediction of drug-target interaction through a rotation forest-based predictor: Lei Wang proposed a computational method for predicting drug–target interactions by combining protein sequence information and drug molecular substructure fingerprints. Protein evolutionary information was represented using Position-Specific Scoring Matrices (PSSM), while drug molecules were encoded as fingerprint feature vectors. Building on this approach, Yu-An Huang later introduced a model using Pseudo Substitution Matrix Representation (Pseudo-SMR) for proteins and

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structure–activity relationship (SAR) features for drugs, along with an Extremely Randomized Trees classifier. The method achieved high prediction accuracy across major target classes, including nuclear receptors, GPCRs, ion channels, and enzymes.

LIMITATIONS: Network pharmacology has significantly advanced drug discovery, but its full potential requires the integration of heterogeneous biological networks and global network information. Such approaches can enhance personalized medicine by enabling the prediction of drug targets, drug resistance, treatment responses, molecular signatures, and cancer risk. The integration of cancer-related networks with sequencing technologies may improve diagnosis, prognosis, treatment, and prevention of cancer. Furthermore, accurate network-based models should incorporate quantitative bioactivity data, robust validation methods, and comprehensive performance evaluation to ensure reliable predictions.

APPLICATIONS

- **Drug Discovery and Development:** Identifies multiple drug targets, enabling the design of safer and more effective therapies.
- **Disease and Cancer Research:** Helps uncover disease mechanisms, cancer-related genes, and signaling pathways involved in complex disorders.
- **Traditional Medicine and Drug Repurposing:** Explains the mechanisms of multi-component herbal medicines and identifies new therapeutic uses for existing drugs.
- **Safety Assessment:** Predicts off-target interactions, toxicity, and adverse drug reactions, improving drug safety and effectiveness.

ADVANTAGES:

1 Better understanding of disease mechanisms
2 Improved drug discovery
3 Supports traditional medicine research
4 Effective for complex diseases

DISADVANTAGES:

1 Dependence of database accuracy
2 Need for experimental validation
3 High computational requirements
4 Requirement of bioinformatics expertise.

NETWORK PHARMACOLOGY IN CANCER: Cancer involves complex network-level alterations in oncogenes, tumor suppressors, transcription factors, kinases, epigenetic regulators, and metabolic enzymes. Network pharmacology helps map these interactions and understand how therapeutic agents modulate cancer-related molecular networks. This approach is particularly valuable because cancer results from dysregulation of interconnected signaling pathways rather than defects in a single gene.

CORE PRINCIPLES APPLIED TO CANCER:

1 Multi-target drug action-anticancer agents act on several proteins
2 Network based disease understanding
3 Pathway enrichment analysis
4 Synergistic mechanisms
5 Prediction of drug resistance mechanisms

SIGNIFICANCE IN MODERN ONCOLOGY RESEARCH

1 Understanding polypharmacology of natural compounds
2 Drug repurposing for oncology
3 Identifying hub genes as therapeutic biomarkers
4 Explaining synergism in combination chemotherapy
5 Studying resistance mechanisms

NETWORK PHARMACOLOGY IN BREAST CANCER: Breast cancer is driven by complex signaling networks, making single-target therapies less effective due to resistance and pathway redundancy. Network pharmacology combined with molecular docking provides a systems-level approach to investigate multi-target therapies. Thymus vulgaris contains bioactive compounds such as thymol, carvacrol, rosmarinic acid, luteolin, and apigenin, which exhibit anticancer, antioxidant, and anti-inflammatory properties. Network analysis suggests that these compounds target key breast cancer-related proteins, including AKT1, EGFR, ESR1, BCL2, and MAPK1, and regulate important pathways such as PI3K-Akt, MAPK, estrogen signaling, and apoptosis.

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Molecular docking further confirms strong binding interactions between thyme phytochemicals and these targets, supporting the potential of Thymus vulgaris a multi-target therapeutic agent against breast cancer.

NETWORK PHARMACOLOGY IN OSTEOSARCOMA:

Osteosarcoma is a common malignant bone tumor that primarily affects adolescents and is characterized by complex molecular alterations involving cell proliferation, apoptosis, inflammation, and angiogenesis. Network pharmacology has been used to investigate the therapeutic potential of Curcuma longa(turmeric), whose major bioactive compounds, including curcumin,demethoxycurcumin,bisdemethoxycurcumin, and turmerones, exhibit favorable drug-like properties. By integrating phytochemical targets with osteosarcoma-associated genes, researchers identified key hub proteins such as AKT1, TP53, MAPK1, CASP3, VEGFA, IL6, and TNF, along with important signaling pathways including PI3K-Akt, MAPK, NF-κB, p53, apoptosis, and HIF-1. Molecular docking studies further demonstrated strong interactions between curcumin and these targets, suggesting that curcuma longa may suppress tumor growth, induce apoptosis, reduce inflammation, and inhibit angiogenesis through a multi-target, multi-pathway mechanism. Together, network pharmacology and molecular docking provide strong evidence supporting the potential of curcumin-rich curcuma longa as an adjunct therapeutic candidate for osteosarcoma.

NETWORK PHARMACOLOGY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE: Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory disorder characterized by chronic airway inflammation and airflow obstruction, commonly caused by cigarette smoke, air pollution, and occupational exposure to harmful particles. Network pharmacology studies have shown that hesperetin, a natural flavonoid, may exert therapeutic effects against COPD by targeting multiple proteins, including ESR1, SRC, PPARG, BCL2, PARP1, KDR, MMP9, and ABCG2. Functional enrichment and pathway analyses revealed that these targets are involved in oxidative stress, inflammation, and key signaling pathways such as MAPK, Ras, and NF-κB. Molecular docking demonstrated strong binding interactions between hesperetin and several hub proteins, supporting its potential to regulate inflammatory and oxidative responses. Experimental studies in COPD mouse models further confirmed that hesperetin improved lung function, reduced inflammatory cell infiltration, lowered pro-inflammatory cytokines (TNF-α, IL-1β, and IL-6), and suppressed MAPK and NF-κB pathway activation. These findings suggest that hesperetin may serve as a promising multi-target natural therapeutic agent for COPD.

NETWORK PHARMACOLOGY IN CORONARY HEART DISEASE:

Coronary heart disease (CHD) is a major cardiovascular disorder caused by atherosclerotic plaque buildup in the coronary arteries, leading to reduced blood flow to the heart and symptoms such as chest pain, shortness of breath, fatigue, and palpitations. Network pharmacology and molecular docking studies have been used to investigate the therapeutic mechanisms of Xuefu Zhuyu Capsule (XFZYC), a traditional Chinese medicine formula widely used for cardiovascular diseases. Analysis identified 139 active compounds and 127 common targets associated with CHD, revealing a multi-component, multi-target mode of action. Key hub proteins, including IL-6, AKT1, STAT3, TP53, VEGFA, and RELA, were found to regulate inflammation, apoptosis, angiogenesis, and vascular remodeling. Pathway enrichment highlighted the involvement of PI3K-Akt, NF-κB, HIF-1, VEGF, FOXO, and IL-17 signaling pathways, which are closely linked to atherosclerosis and vascular inflammation. Molecular docking demonstrated strong binding interactions between major compounds such as quercetin, kaempferol, luteolin, nobiletin, and β-sitosterol and the core target proteins, supporting the hypothesis that XFZYC exerts cardioprotective effects by simultaneously

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modulating multiple molecular targets and signaling pathways involved in CHD progression.

NETWORK PHARMACOLOGY IN POLYCYSTICOVARIAN SYNDROME: Polycystic Ovary Syndrome (PCOS) is a common endocrine and metabolic disorder characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology. Using a network pharmacology approach, researchers investigated the therapeutic potential of Sutaehwan (STH), a traditional Korean herbal formulation. Protein–protein interaction and enrichment analyses identified key targets involved in ovarian steroidogenesis, cell-cycle regulation, and endocrine signaling, with Anti-Müllerian Hormone (AMH) and its receptor AMHR2 emerging as central regulators. Experimental validation in a letrozole-induced PCOS rat model demonstrated that STH restored estrous cyclicity, reduced ovarian cysts, improved ovarian and uterine morphology, and enhanced ovulatory function. Molecular analyses further showed that STH significantly down regulated AMH and AMHR2 expression, suggesting that it alleviates follicular arrest and promotes normal follicular development. These findings indicate that Sutaehwan may improve PCOS through multi-target regulation of the AMH–AMHR2 signaling pathway, highlighting its potential as a complementary therapeutic strategy and demonstrating the value of network pharmacology in validating traditional herbal medicines.

II. DISCUSSION:

Network pharmacology is a systems-level approach that integrates pharmacology, bioinformatics, and systems biology to understand how drugs act on multiple targets and pathways within complex biological networks. By combining database mining, network construction, pathway enrichment, molecular docking, and experimental validation, it provides a comprehensive framework for identifying therapeutic targets, elucidating drug mechanisms, and supporting drug discovery and precision medicine.

Applications of network pharmacology have demonstrated the therapeutic potential of natural compounds and herbal formulations in diseases such as breast cancer, osteosarcoma, COPD, coronary heart disease, and PCOS. Studies involving Thymus vulgaris, curcuma longa hesperetin, Xuefu Zhuyu Capsule, and Sutaehwan revealed their ability to regulate multiple disease-related targets and signaling pathways. Molecular docking further validated these interactions, highlighting the value of network pharmacology in understanding multi-target therapies and advancing the development of effective treatments for complex diseases.

III. SUMMARY:

Network pharmacology provides a system-level framework to understand how multi-component therapeutics modulate complex disease networks through multi- target interactions.In cancers such as breast cancer and osteosarcoma , it reveals how phytochemicals (thyme oil constituents and curcuma derivatives)influence apoptosis, cell cycle regulation and tumour signaling networks through pathways like P13K/Akt and MAPK. In chronic respiratory disorder like COPD compound such as hesperetin are shown through network mapping and molecular docking –to regulate inflammatory mediators , oxidative stress and cytokine signalling. For cardiovascular condition like coronary heart disease ,formulation such as xuefu zhuyu capsule are analysed to uncover multi-target effects on blood circulation , lipid metabolism and endothelial function. Similarly, in polycystic ovarian syndrome, herbal formulation like sutaehwan are explored for their role in modulating hormonal signaling pathway , particularly AMH-AMHR2 interactions. pathway analysis and molecular validation to elucidate the the holistic therapeutic mechanisms of complex interventions across diverse disorders.

IV. CONCLUSION:

Network pharmacology offers a powerful system- level strategy to decode how multi-component therapies act on complex disease networks across breast cancer, osteosarcoma, chronic obstructive pulmonary disease (COPD), Coronary heart disease, polycystic ovarian syndrome. By

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integrating target prediction interaction networks, pathway enrichment , molecular docking and experimental validation , it reveals how bioactive compounds simultaneously modulate interconnected pathways related to inflammation, apoptosis, oxidative stress, metabolism and hormonal regulation, thereby supporting the development of evidence-based, multi- target therapeutic strategies for complex chronic disorders.

REFERENCE:

[1]. Hopkins AL. Network pharmacology; the next paradigm in drug discovery. Nat chem. 2008;4(11):682-690.
[2]. Hopkins AL. Network pharmacology.NatBiotechnol.2007;25(10):1110-1111
[3]. Li S.Zhang B. Traditional Chinese medicine network pharmacology :theory, methodology and application .Chin J Nat Med. 2013;11(2):110-120
[4]. Yaminishi Y.Araki M, gutteridge A. Honda W, Kanehisa M. prediction of drug-target interaction networks from the integration of chemical and genomic spaces.Bioinformatics.2008;24(13):i232 i240.
[5]. Lun Yang, chen J. Chemical –protein interactome and its application in drug discovery and adverse drug reaction prediction . 2014;15(4):552-564
[6]. Bleakley K, Yamanishi Y.Supervised prediction of drug –target interactions using bipartite local models. Bioinformatics.2009;25(18):2597- 2403
[7]. Keiser MJ,Setola V, Irwin JJ, Laggner C, Abbas AI, Hufeisen SJ . Predicting new molecular targets for known drugs.2009;462(7270):175-181.
[8]. Houghton, S. C, Hankinson S.E. Cancer progress and priorities: breast cancer Epidemiol.2021;30(5):822-844.
[9]. Salehi B,Mishra AP, Shukla I, Sharifi –Rad M. Contreras M del M, Segura –carretero A.Thymol . thyme and other plant sources :health and potential uses. Phytother Res .2018;32(9):1688-1706
[10]. Meng XY, Zhang HX, Mezei M, Cui M. Molecular docking :a powerful approach for structure –based drug discovery.curr comput Aided drug.2011 ;7(2):146-57
[11]. Aggarwal BB, Harikumar KB, Potential therapeutic effects of curcumin. the anti-inflammatory agent, against cancer .Int J Biochem cell.2009; 41(1):40-59
[12]. Mirabello L, Troisi RJ , Savage SA. Osteosarcoma incidence and survival rates from 1973 to 2004. Cancer.2009;115(7):1531-43.
[13]. Tomeh MA, Hadianamrei R, Zhao X. A review of curcumin and its derivatives as anticancer agents.2019;20(5):1033
[14]. Barnes PJ. Inflammatory mechanisms in patients with chronic obstructive pulmonary disease. J Allergy clin immunol.2016;138(1):16-27
[15]. Parhiz H, Roohbakhsh A, Soltani F, Rezaee R, Iranshahi M. Antioxidant and anti-inflammatory properties of the citrus flavanoids hesperidin and hesperetin :an updated review of their molecular mechanisms and experimental models. phytother . 2015;29 (3):323-31
[16]. Hansson GK . Inflammation , atherosclerosis, and coronary artery disease. N Engl J Med.2005;352(16):1685-95
[17]. Ferrara N. VEGF and the quest for tumour angiogenesis factors. Nat Rev Cancer.2002;2(10):795-803
[18]. Azziz R,Carmina E,Chen Z ,Dunaif A, Laven JS, Legro RS. Polycystic ovary syndrome.Nat Rev Dis Primers.2016;(2) :16057
[19]. Kim JH, Lee JH, Lee HJ, Song YS. Herbal medicine (sutaehwan) for ovarian function and infertility: experimental and clinical perspectives .J Ethnopharmacol.2017;206:292-301.
[20]. Liu Z, Zhang Y, Li Y, Xiao Y, Zhang Q. Multi- target effects of herbal medicines on polycystic ovary syndrome :a systems pharmacology approach. Front Pharmacol.2020;11:563.